United States Patent [19]

Sundeen et al.

[11] **4,382,081**

[45] * **May 3, 1983**

[54] **INHIBITORS OF MAMMALIAN COLLAGENASE**

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[*] Notice: The portion of the term of this patent subsequent to Nov. 25, 1997, has been disclaimed.

[21] Appl. No.: **273,142**

[22] Filed: **Jun. 12, 1981**

[51] **Int. Cl.**[3] **A61K 37/00**; C07C 103/52

[52] **U.S. Cl.** ..... **424/177**; 260/112.5 R

[58] **Field of Search** ..... 424/177; 260/112.5 R

[56] **References Cited**

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"Structure-Inhibition Relationships Among Metal--binding Collagen Peptide Analogues", Hossain Saneii* and Arno F. Spatola* (SPON: John W. Brown), University of Louisville, Louisville, KY 40292, May 1, 1981, vol. 40, No. 6.

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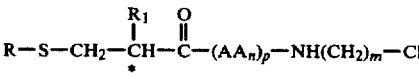
[57] **ABSTRACT**

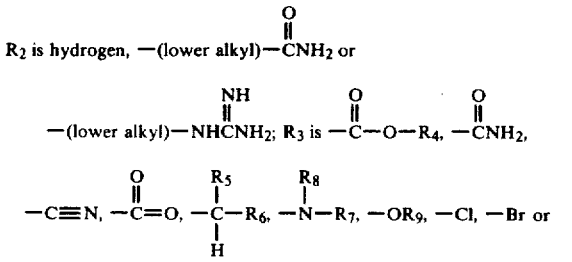
Mammalian collagenase is inhibited by compounds of the formula



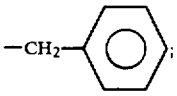
or salts thereof, wherein

R is hydrogen, alkanoyl of 2 to 10 carbon atoms or arylcarbonyl;

R_1 is of 3 to 8 carbon atoms, cycloalkyl of 3 to 7 carbon atoms, aryl or arylalkyl;



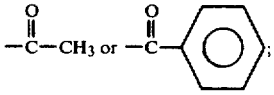
R_4 is hydrogen, methyl, ethyl, or



R_5 and R_6 are each independently selected as $-OCH_3$ or $-OCH_2CH_3$ or are combined as $-OCH_2CH_2O-$ or $-O-(CH_2)-O-$;

R_7 and R_8 are each independently selected as hydrogen, methyl or ethyl or are combined as $-(CH_2)_4-$, $-(CH_2)_5-$ or $-CH_2CH_2-O-CH_2CH_2-$;

R_9 is hydrogen, methyl, ethyl



m is an integer from 0 to 7; p is an integer from 1 to 3;

AA_n is an amino acid chain of from one to three amino acids; n is 1 or 1, 2 or 1, 2, 3;

when p is 1, AA_n is AA_1;

when p is 2, AA_n is AA_1—AA_2;

when p is 3, AA_n is AA_1—AA_2—AA_3;

AA_1 is glycine or alanine;

AA_2 is glycine or alanine;

AA_3 is leucine, glutamine or isoleucine.

A method of reducing the adverse effects of mammalian collagenase in a mammalian host in need thereof, which comprises administering to the mammal an effective amount of a compound having the above formula is within the scope of the invention.

10 Claims, No Drawings